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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/027,671	02/23/1998	ALAN K. SMITH	4292-0048-55	3507

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/027,671	SMITH ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *95-113* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *95-113* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The **examiner** of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michail Belyavskyi, Group Art Unit 1644, Technology Center 1600.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/14/06 has been entered.

3. Claims 95-113 are pending

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

5. It is noted that the Brief Description of the Figures, disclosed Figure 1, panels A-D, Fig.2 panel A-B; Fig.3, panel A-B and Fig.4, panel A-B. There is no said panels in the submitted figures.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7 . Claims 95-113 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a method of obtaining a human T lymphocytes with enhanced replicative potential comprising culturing said cells under conditions including replacement of a liquid culture at a rate of from 50% to 100 % daily replacement compared to replicative potential of a human T lymphocytes culturing ex vivo under conditions which do not include replacement of the liquid culture medium, does not reasonably provide enablement for a method for

obtaining a human cells with enhanced of *any* biological function , wherein said human cells are recited in claim 95, compared to the biological function of said cells cultured ex vivo under conditions which do not include replacement of the liquid culture medium, claimed in claims 95-113. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims as written encompass the genus of cells with enhanced biological function human cells recited in claim 95 , wherein said function are not even defined in the Specification.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claims, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses detailed *in vitro* studies wherein human T lymphocytes and human dendritic cells grown under continuous perfusion of medium resulted in high density of concentrations, i.e. enhanced replicative potential (see Example 1-3 in particular) and The Specification defined biological function as " the ability of a cell population to carry outs its biological mission, i.e. to performed its recognized biological purpose *in vivo*" (see overlapping pages 10- 11 of the instant specification in particular.) However, it is noted that the specification does not adequately teach how to effectively obtained a human cells with enhanced of *any* biological function , wherein said human cells are recited in claim 95 compared to the biological function of said cells wherein said cells cultured ex vivo under conditions which do not include replacement of the liquid culture medium. Moreover, the Specification does not even define what biological function, besides stimulating activity of dendritic cells *in vitro,* would be enhanced. Applicant has not exemplified any *in vivo or in vitro* studies, wherein claimed method results in enhanced of *any* biological function of human cells recited in claim 95. Moreover, no animals models were used to show that said lineage committed dendritic cells would maintained or preserved its enhanced biological function when administering back into mammals. Peshwa (WO'97/03186) teaches that there appear to be significant differences in the characteristics of function and properties of human cells (see entire document, page 2 in particular). Engleman (WO 97/22349) teaches that biological properties of human cells are unpredictable and , depending on culturing and growth conditions, can be different. Engleman further stresses that *in vitro* data about biological function of human dendritic cells does not always correlate with *in vivo* results (see entire document, page 6 in particular) . In addition, Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to *in vitro* models and partly animal-human xenograft systems, tissue cells in vivo seems to express molecules for defense against

cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously *in vitro* but a fairly high portion of them still fail *in vivo.*

Since there are no *in vivo* studies or data in the specification to show the effectiveness of maintaining or preserving any enhanced biological function of human cells recited in claim 95, it is unpredictable as to how to correlate *in vitro* results with *in vivo* use. Although the Specification describes certain *in vitro* experiments, there is no correlation on this record between *in vitro* experiments and *in vivo* data of the method of obtaining and maintaining an enhanced any biological function of human cells recited in claim 95 comprising replacement of a liquid culture medium at a rate of from 50% to 100% daily replacement . It is not enough to rely on *in vitro* studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to efficacy in humans or animals.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed a method for obtaining a human cells with enhanced of *any* biological function , wherein said human cells are recited in claim 95, compared to the biological function of said cells cultured ex vivo under conditions which do not include replacement of the liquid culture medium, claimed in claims 95-113 in a manner reasonably correlated with the scope of the invention. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 95-113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al., (Blood, 1997, V.90, NO.10 page 347B,) or US Patent 5,994,126 .

Smith et al., teach method of obtaining a composition comprising human dendritic cells , wherein said cells are antigen primed dendritic cells, with exhibiting enhanced biological function *in vitro* as compared to the biological function of the lineage commited dendritic cells cultured ex vivo under condition which do not include replacement of the liquid culture (see entire document). Smith et al., teach a growth condition wherein culture medium is continuously perfused. Smith et al., teach that continues medium perfusion at an innoculum density of 1.6×10^{6} cells/ ml enhanced biological function of harvested dendritic cells.

US Patent '126 teaches method of obtaining composition comprising lineage committed human dendritic cells , wherein said cells are antigen primed dendritic cells, cultured ex vivo under condition wherein the liquid cultured medium is replaced (see entire document, column 13, lines 10-25, column 15, line 54-65 and column 21, line 29-35 in particular. US Patent '126 teachers that media replaced every other day for about $5x10^{5}$ cells/ml culture(see column 17, lines 60-65 and Example 1 in particular). It is noted that US Patent '126 teaches does not explicitly teaches that said cells have an enhanced biological function as compared to the function of the lineage committed cell cultured *ex-vivo* under conditions which do not include replacement of the liquid culture. However, it is noted that the referenced cells were obtained from the same sources and cultured under the same culturing conditions as claimed thus obviously would have an enhanced biological function *in vitro*. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed.

The claimed invention differs from the reference teaching in that the Smith et al., and US Patent '126 do not explicitly teach that the culture medium is replaced daily at the rate of at least 25%, or 50% or 25 to 100% .

It is noted however, that prior art references teach a culturing condition, wherein the medium is continuously perfused. In other words, they teach the culturing condition wherein culture medium is replaced. Moreover, Smith et al., further teach that said continuously perfused system was set to evaluate the effects of frequent medium exchange on dendritic cell expansion and biological function. In other words, culturing under growth conditions wherein the growth medium is replaced have an effect on biological function of cultured cells Thus, it would require only routine experimentation for a person of ordinary skill in the art to determine the optimum rate of replacement of the medium, i.e. at a rate of 25% or 50% or from 25% to 100% . Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

One of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention because according to Smith et al., there is a direct correlation between the biological function of dendritic cells and the culturing condition comprising the replacement of a liquid culture medium during the culturing.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 95-113 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,835,566. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-18 of U.S. Patent No. 6,835,566 recites a method of obtaining a lineage-committed dendritic cell exhibiting enhanced biological function, comprising culturing said cells under condition of replacement culture medium at a rate from 25% to 100% daily. Though claims 1-18 of U.S. Patent No. 6,835,566 do not explicitly recites specific type of the cells, as in claim 95, it would be immediately obvious to one skill in the art , to substitute a lineage-committed dendritic cell of claims 1-18 of U.S. Patent No. 6,835,566 with cells recited in instant claim 95.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER
11/24/06